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Session: Virology and Viral Infections (Non-HIV)
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Fulminant hepatitis E in pregnancy: a rare case of success

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Background: Fulminant hepatic failure (FHF) refers to the rapid development of severe acute liver injury with encephalopathy in a person who previously had a normal liver. Hepatitis E virus infection is an important cause of severe clinical FHF in pregnant women and is associated with high mortality (15-25%).

Methods: A 40-year-old sub-Saharan African woman (Gesta5, Para4), in the third trimester of pregnancy and just arrived from Angola, was admitted to our hospital with a 3 weeks history of astenia, nausea and abdominal pain. Her past history was positive for high blood pressure. Her medications included methyldopa (500mg QID) and Sulfadoxine and Pyrimethamine (malaria intermittent preventive treatment).

Results: On physical examination, the patient was alert, with no signs of distress, slightly jaundiced, presenting a diffuse tenderness to palpation of the right upper quadrant. Laboratory values showed an AST and ALT above 50 times normal, a bilirubin level of 6.6 mg/dL and an INR of 2,8.

Conclusion: Progressive decline in liver synthetic function was observed and 48 hours after admission, MELD's, Clichy's and King's College Hospital criteria for liver transplant were fulfilled. The patient was transferred to a transplantation centre and within 2 days an appropriate liver allograft became available. A combined cesarean delivery and orthotopic liver transplantation were successfully performed. Acetaminophen measurement was negative, hepatitis A, B, C, HIV and CMV serology were negative, antibody panel for autoimmune hepatitis was negative, ceruloplasmin level was normal. Finally, the diagnosis was made when high titers of IgG and IgM anti-HEV were detected.

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Rare complication to acute bronchiolitis

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Background: Two infants presented with acute bronchiolitis and proceeding significant pneumatoceles. We present their management, subsequent investigation and progress.

sive outcome was a clinical characteristic, with severe acute respiratory insuficiency. Radiological findings was a large hyperlucency in the left superior pulmonary lobe. The patient received i.v.antibiotherapy, oxygen, digoxin. In the tenth day the patient is transferred in surgery department, where a large pulmonary cyst (8/9 cm) was removed.

Case 2: a 6-months old infant was admitted for a moderate acute bronchiolitis. He was born prematurely, at 28 weeks of gestation and he needed ventilation support for 72 hours after birth. Radiological study identified 2 hyperlucent images (pneumatoceles) in the medium right pulmonary lobe. He left the hospital in the 12th day of life. After 4 days from the discharge he had fever and dyspneea. Repeated pulmonary X-ray revealed extension of pulmonary cysts, observation confirmed also by pulmonary CT. Surgical diagnosis was of pneumatoceles.

Results: Pneumatoceles are very rare complication of bronchiolitis. Multiple sources recognize their association with bacterial pneumonia, but none supports a link to bronchiolitis.

Conclusion: A rare complication of an apparently common disease imposes a more complex study for identification of an underlying disease.

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Early predictors of severe dengue in adults

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Background: Dengue is the main infectious disease causing high morbidity and mortality among adults in dengue endemic regions of Sri Lanka. Prediction of severe illness at an earlier stage of infection helps to arrive at management decisions. Studies to identify predictors of severe dengue in adults are sparse.

Methods: In order to identify predictors of severe dengue by the third day of illness, symptoms, signs and investigation results of first 3 days of illness between two groups A and B (defined below) were compared in a prospective cohort study of consecutive 117 adult patients (age>12 years) with serologically confirmed dengue admitted to the professorial medical unit, Colombo North Teaching Hospital, Ragama, Sri Lanka over 6 month from 1st of March 2011. Group A (Severe illness): development of ascites or pleural effusions (evidence of fluid leakage), compensated shock and profound shock (as defined by WHO guidelines for Dengue 2010), Group B: all others who did not fall into Group A. Severity of symptoms was assessed by a visual analogue scale, and rest of the clinical parameters, investigation results were documented prospectively.

Results: Of the 117 adults (95 males) mean age 31.95years (SD=13.34); 27 fell into Group A and 90 into group B. On the 3rd day of illness, mean Aspartate aminotransferase (AST); Group A 260 iu/L (SD=168.8) vs Group B-145 iu/L (SD=135.11) (p=0.005). Mean Alanine aminotransferase (ALT); Group A-247 iu/L (SD=161.5) vs

Group B-105iu/L (SD-91.5) (p=0.002). None of the symptoms, signs and other investigations including platelet count, packed cell volume (PCV) and white blood cell count was significantly different. Analysis of the whole 117, pearson correlation test showed a positive correlation of AST(r=0.3) (p=0.038) and ALT(r=0.3) (P=0.045) with PCV and a negative correlation (r=-0.3) with platelet count (p=0.014). AST(r=0.25) and ALT (r=0.3) on day 3 was positively correlated with development of malena at any stage (p=0.05).

Conclusion: Higher AST and ALT levels on 3rd day of dengue seems to be useful predictors of severe dengue.

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Phenotypic and functional characterization of human γδ T cell subsets in response to influenza A viruses

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Background: It has become increasingly clear that γδ T cells are important components in both innate and adaptive immune systems, yet the cellular requirement for the activation of γδ T cells is still poorly defined. Like αβ T cells, human Vγ9Vδ2 T cells may be divided into four subsets: naive, central memory, effector memory and terminal differentiated cells, according to their surface expression of CD45RA and CD27. Whether human Vγ9Vδ2 T cells have functionally different subsets in response to influenza A (fluA) viruses remains unknown.

Methods: Here we applied fluA virus-infected primary human monocyte-derived macrophages (MDMs) for examining the antiviral activity of phosphoantigen isopentenyl pyrophosphate (IPP)-expanded human Vγ9Vδ2 cells against influenza viruses. Different γδ T subsets were sorted with FACS Aria-II dependent on the surface expression levels of CD27 or CD56. Flow cytometry was used for phenotyping, cytotoxic assay and cytokine quantification. Specific blocking antibodies were utilized to uncover the mechanisms for γδ-T-mediated cytolytic antiviral effects.

Results: In this study, we demonstrated that both central (CD45RA-CD27+) and effector (CD45RA-CD27-) memory Vγ9Vδ2 T had similar levels of immediate IFN-γ and cytotoxic responses to human and avian fluA virus-infected cells. In contrast, CD56+ Vγ9Vδ2 T cells had significantly higher cytotoxicity against fluA virus-infected cells, compared with CD56- counterparts, while both subsets had similar IFN-γ responses. We further demonstrated that the CD16-dependant degranulation pathway, but not antibody-dependent cell-mediated cytotoxicity (ADCC), contributed to the superior cytotoxicity of CD56+ Vγ9Vδ2 T cells.

Conclusion: Our study provides further evidence for the phenotypic and functional characterization of human Vγ9Vδ2 T subsets during fluA virus infection, and may help improve the γδ T cell-based immunotherapy for viral infection. As γδ T cell-based immunotherapy has been showed a great potential for treating fluA infection, our findings may help improve its efficacy for the control of viral infection.

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Unscrambling Potential Biomarkers To Differentiate Dengue Hemorrhagic Fever From Dengue Fever

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Background: Dengue virus (DENV) infection is a re-emerging infectious disease that accounts for hundred million cases annually. However, there are no vaccine and effective therapeutic options currently available. Early recognition and prompt supportive treatment can help to lower the risk of developing severe disease complications such as Dengue Hemorrhagic Fever/Dengue Shock Syndrome (DHF/DSS). Hence there is an urge to identify the biomarkers linked with DHF/DSS. Thus, this study aimed to identify potential biomarkers that are linked with varying degrees of disease severity and capable of differentiating Dengue Hemorrhagic Fever/Dengue Shock Syndrome (DHF/DSS) and Dengue fever (DF).

Methods: The sera samples collected from dengue patients with varying degrees of disease severity DF, DHF and DSS) were used to probe the protoarray chips containing 9000 human proteins (Invitrogen). The sera samples were collected at three different time points from each patient (first sample: 1-4 days; second sample: 5-7 days; third sample: 21 days). After probing with appropriate antibodies, the protoarray chips were scanned in a microarray scanner. Data analysis was performed using protoarray prospector software (Invitrogen).

Results: A wide range of proteins involved in signal transduction, membrane permeability, intracellular trafficking, enzymatic activity, transcription, muscle functions, immune response and apoptosis were found to be stimulated during dengue infection. Interestingly, proteins related to vascular permeability (EGF-like domain-containing protein 7, α-macroglobulin and *vascular endothelial growth factor*) were identified in DHF sera. Although, these results were derived from 14 dengue sera, the results were consistent. The authenticity of the identified biomarkers were analysed using 100-150 serum samples obtained from Dengue patients with varying degrees of disease severity. The results reaffirmed that *vascular endothelial growth factor* and α-macroglobulin were present at a significantly higher quantities (P<0.05) in the serum samples of DHF/DSS patients compared to that of DF patients. This assures that *vascular endothelial growth factor* and α-macroglobulin can be used as biomarkers to differentiate DHF/DSS from DF.

Conclusion: Identification of these attractive biomarkers associated with severe disease development would help in administrating appropriate supportive treatment which in turn lead to decreased hospitalization rate and reduce healthcare cost.

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